12. (Amended) A process for producing a sustained drug release product comprising impregnating the pores of the porous spherical-shape bio-ceramics obtained according to claim 1 or 2 with a drug.

13. (Amended) A process as claimed in claim 12, wherein, after the drug is impregnated into the porous bio-ceramics, the impregnated parts are plugged by said bio-ceramics, whereby the sustained release time of the drug is controlled.

14. (New) A process as claimed in claim 1, wherein the binder slurry is an aqueous solution of one or more of a water-soluble cellulose derivative, polyvinyl alcohol, polyacrylic acid, polyacrylamide, polyvinyl pyrrolidone, polyethylene glycol, and starch.

15. (New) A process as claimed in claim 1, wherein the starting material is added dropwise to liquid nitrogen from a thin tube having an inner diameter of 0.2 to 2 mm.

REMARKS

Claims 1 to 5 and 11 to 15, as amended, are pending. Applicants have amended claims 1 to 5 and 11 to 13, and added new claims 14 and 15. Attached hereto is a marked-up version of the changes made to the above-identified application by the current amendment, which is captioned "**Version with markings to show changes made**." The amendments find full support in the original specification and claims. Specifically, the amendments to claims 1 and 5 find support in the English translation at page 6, line 20, to page 7, line 1. New claim 14 finds support in the English translation at page 6, lines 27 to 32. New claim 15 finds support in the English translation at page 7, lines 11 to 18. No new matter is presented.

The Examiner rejected claims 1, 2, 5, and 11 under 35 U.S.C. § 102(b) as allegedly anticipated by Schumacher (DE 3835728 A1). Applicants respectfully traverse this rejection.

Independent claims 1 and 5 are directed to a process for producing porous spherically-shaped bio-ceramics. The process recited in claim 1 comprises dropping a starting material for ceramics into a low temperature medium, followed by freeze drying and then sintering the same, wherein the starting

material is obtained by adding, to a calcium phosphate in the form of a powder having a size of not more than 100 μm, a 3 to 15% by weight aqueous solution of a binder in an amount of 2 to 4 times the weight of the powder. Claim 5 recites similar limitations. The inventive process produces bio-ceramics having a spherical shape and a larger size, for example, about 10 mm, with a uniform porosity. Such a larger size particle is particularly useful for the preparation of bone filler and other biorepair materials and for impregnating a drug into the pores of such materials.

Schumacher does not teach or suggest the claimed process. Schumacher discloses the production of particles of a size from 1 to 1000 nm by atomizing a solution containing the ceramic material in a cold reactor to freeze the droplets, followed by freeze drying and sintering. However, Schumacher neither teaches nor suggests the use of a starting material obtained by adding, to a calcium phosphate in the form of a powder having a size of not more than 100 μm, a 3 to 15% by weight aqueous solution of a binder in an amount of 2 to 4 times the weight of the powder. Accordingly, Schumacher does not anticipate the claimed process, and Applicants request that the rejection over Schumacher be withdrawn.

The Examiner rejected claims 1 to 5 and 11 to 13 under 35 U.S.C. § 103(a) as allegedly unpatentable over Urist (U.S. Patent No. 4,596,574) in view of Gombotz et al. (U.S. Patent No. 5,019,400) further in view of Schumacher or Reetz et al. (DE 4118752A1). Applicants respectfully traverse this rejection.

Urist discloses a composition comprising a physiologically acceptable, biodegradable porous ceramic containing bone morphogenic protein (BMP) obtained by contacting a physiologically acceptable, biodegradable porous ceramic with a liquid containing substantially pure BMP and removing the liquid therefrom so that an effective amount of BMP is entrapped in the porous ceramic. As acknowledged by the Examiner, Urist does not teach the method of making the porous ceramics. Moreover, Urist does not teach or suggest the production of spherically-shaped bio-ceramics having the controlled size according to the present invention.

Gombotz discloses the preparation of polymeric microspheres for controlled release of substances by atomizing the droplets of polymer solution into a liquified gas, followed by thawing the polymer solvent in the frozen droplets of polymer solution. Gombotz nowhere teaches or suggests the use of a starting material obtained by adding, to a calcium phosphate in the form of a powder having a

size of not more than 100 μm, a 3 to 15% by weight aqueous solution of a binder in an amount of 2 to 4 times the weight of the powder, as presently claimed.

Reetz discloses a method of dropping ceramic material into a liquid cooling medium, freeze-drying the granule, and then sintering to form a spherical particle having a size of 0.04 to 0.4 mm. However, Reetz neither teaches nor suggests the use of a starting material obtained by adding, to a calcium phosphate in the form of a powder having a size of not more than 100 μm, a 3 to 15% by weight aqueous solution of a binder in an amount of 2 to 4 times the weight of the powder. As noted above, Schumacher similarly does not teach or suggest this limitation.

Thus, none of the cited references teach or suggest the use of a starting material obtained by adding, to a calcium phosphate in the form of a powder having a size of not more than 100 μm, a 3 to 15% by weight aqueous solution of a binder in an amount of 2 to 4 times the weight of the powder, as presently claimed. Accordingly, the cited references, even in combination, do not render unpatentable independent claims 1 and 5 or any claims depending therefrom. Applicants therefore respectfully request that the rejection under section 103(a) be withdrawn.

In view of the foregoing amendments and remarks, Applicants respectfully submit that claims 1 to 5 and 11 to 15, as amended, are in condition for allowance, and a timely indication of allowance is respectfully requested. If there are any remaining issues that can be addressed by telephone, Applicants invite the Examiner to contact the undersigned at the number indicated below.

Respectfully submitted,

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By _____

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims:

Please amend claims 1 to 5 and 11 to 13 as follows:

1. (Twice Amended) A process for producing porous spherically-shaped bio-ceramics comprising dropping a starting material for ceramics into a low temperature medium, followed by freeze drying and then sintering the same, wherein the starting material is obtained by adding, to a calcium phosphate in the form of a powder having a size of not more than 100 μm, a 3 to 15% by weight aqueous solution of a binder in an amount of 2 to 4 times the weight of the powder.

2. (Twice Amended) A process for producing porous spherically-shaped bio-ceramics as claimed in claim 1, wherein the [~~starting material is~~] calcium phosphate is hydroxyapatite, tricalcium phosphate, calcium dihydrogenphosphate, tetracalcium phosphate, octacalcium phosphate, or a mixture [~~of these calcium phosphates~~] thereof.

3. (Twice Amended) A sustained drug release product obtained by forming the porous spherical-shape bio-ceramics obtained according to claim 1 or 2, [~~into a porous product, followed by impregnating the pores~~] wherein the pores are impregnated with a drug.

4. (Twice Amended) A sustained drug release product as claimed in claim 3, wherein, after the drug is impregnated into the porous bio-ceramics, the impregnated parts are plugged by said bio-ceramics, whereby the sustained release time of the drug is controlled.

5. (Twice Amended) A process for producing porous spherically-shaped bio-ceramics comprising:

bringing a starting material for bio-ceramics into contact with a low temperature medium, wherein the starting material is obtained by adding, to a calcium phosphate in the form of a powder having a size of not more than 100 μm, a 3 to 15% by weight aqueous solution of a binder in an amount of 2 to 4 times the weight of the powder, followed by freeze drying to form a freeze dried product and;

thereafter sintering the resultant freeze dried product.

11. (Amended) A process for producing porous spherically-shaped bio-ceramics as claimed in claim 5, wherein the [~~starting material is~~] calcium phosphate is hydroxyapatite, tricalcium phosphate, calcium dihydrogenphosphate, tetracalcium phosphate, octacalcium phosphate, or a mixture [~~of these calcium phosphates~~]thereof.

12. (Amended) A process for producing a sustained drug release product comprising [~~forming~~] impregnating the pores of the porous spherical-shape bio-ceramics obtained according to claim 1 or 2 [~~into a porous product and by impregnating the pores~~] with a drug.

13. (Amended) A process as claimed in claim 12, wherein, after the drug is impregnated into the porous bio-ceramics, the impregnated parts are plugged by said bio-ceramics, whereby the sustained release time of the drug is controlled.

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